A Volumetric Growth Model for Healing Post-Infarction Scar

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Background

Remodeling of Damaged Infarct Scar Region

Block in Artery

Heart Attack [1]

Muscle Damage
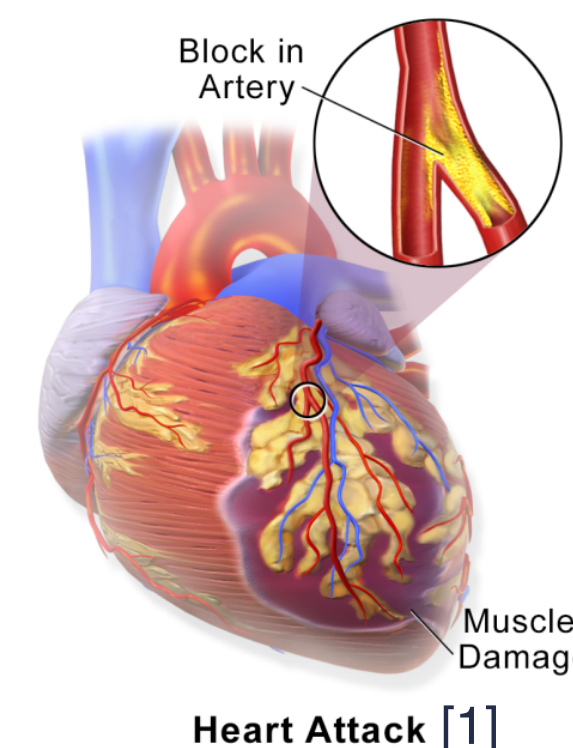
↑ Tissue Stiffness
↓ Tissue Volume [2,3]

Geometric Changes During Scar Healing

In-Plane Dimension Ratio

Thickness Ratio

Time (Week): < 2, 2-4, > 4

Compaction ←→ Expansion   Thinning ←→ Thickening [4]
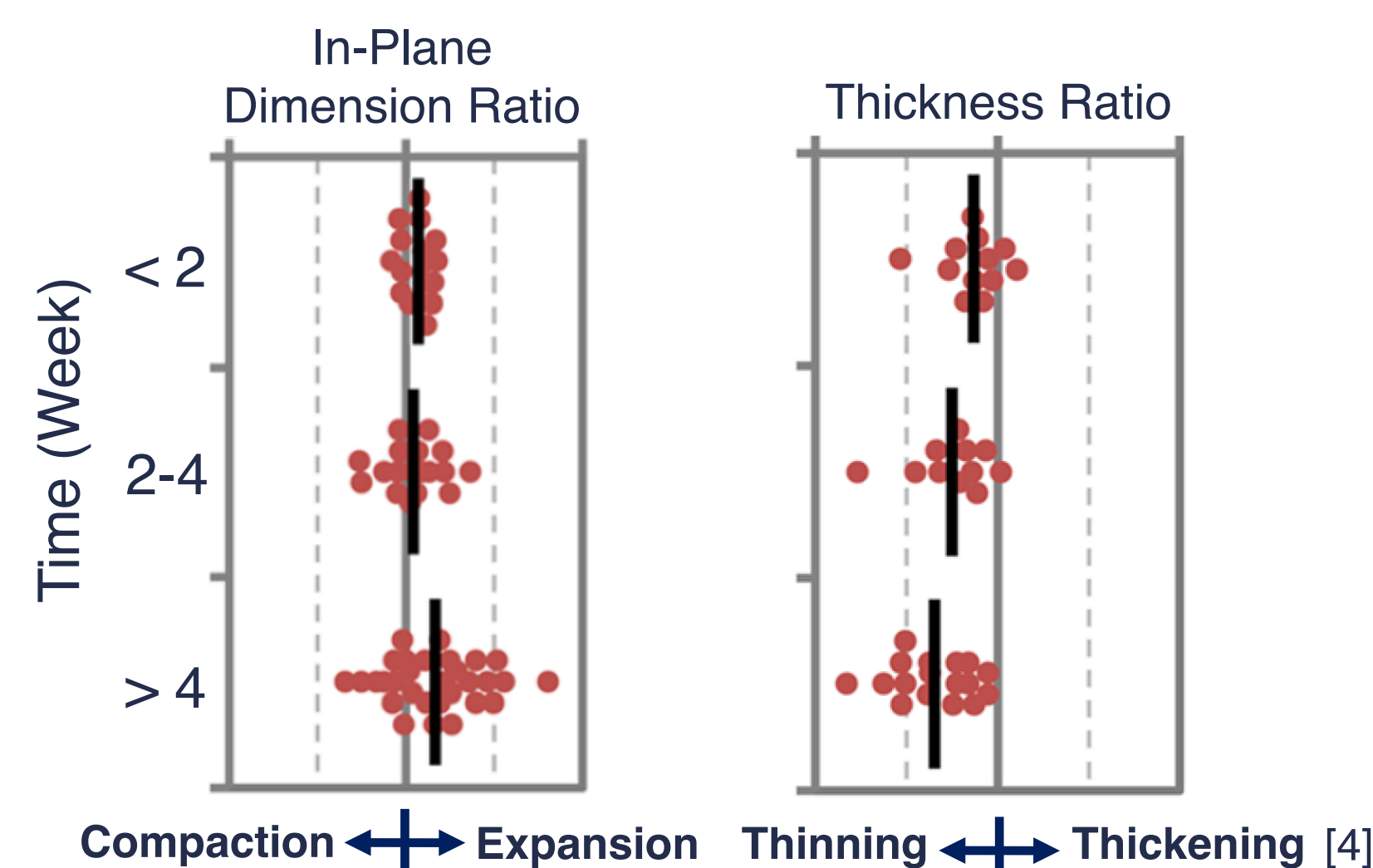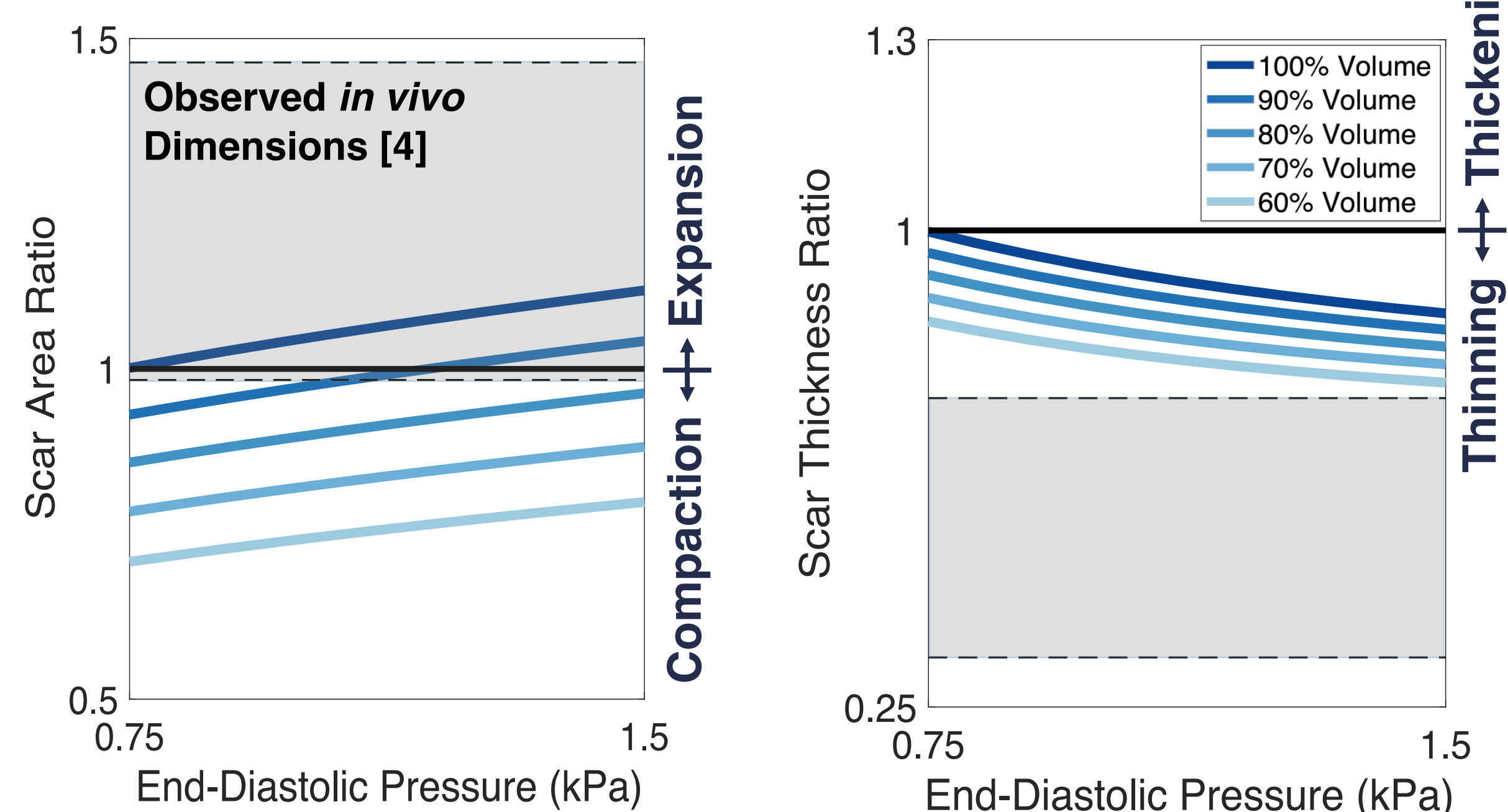
Objective: To better interpret these reports and separate the contributions of volumetric loss, scar stiffening, and elevated diastolic pressures (EDPs) typical after MI, we employed a finite-element model and attempted to reproduce observed changes in *in vivo* scar dimensions assuming volume loss in the scar occurs isotropically in the unloaded state.
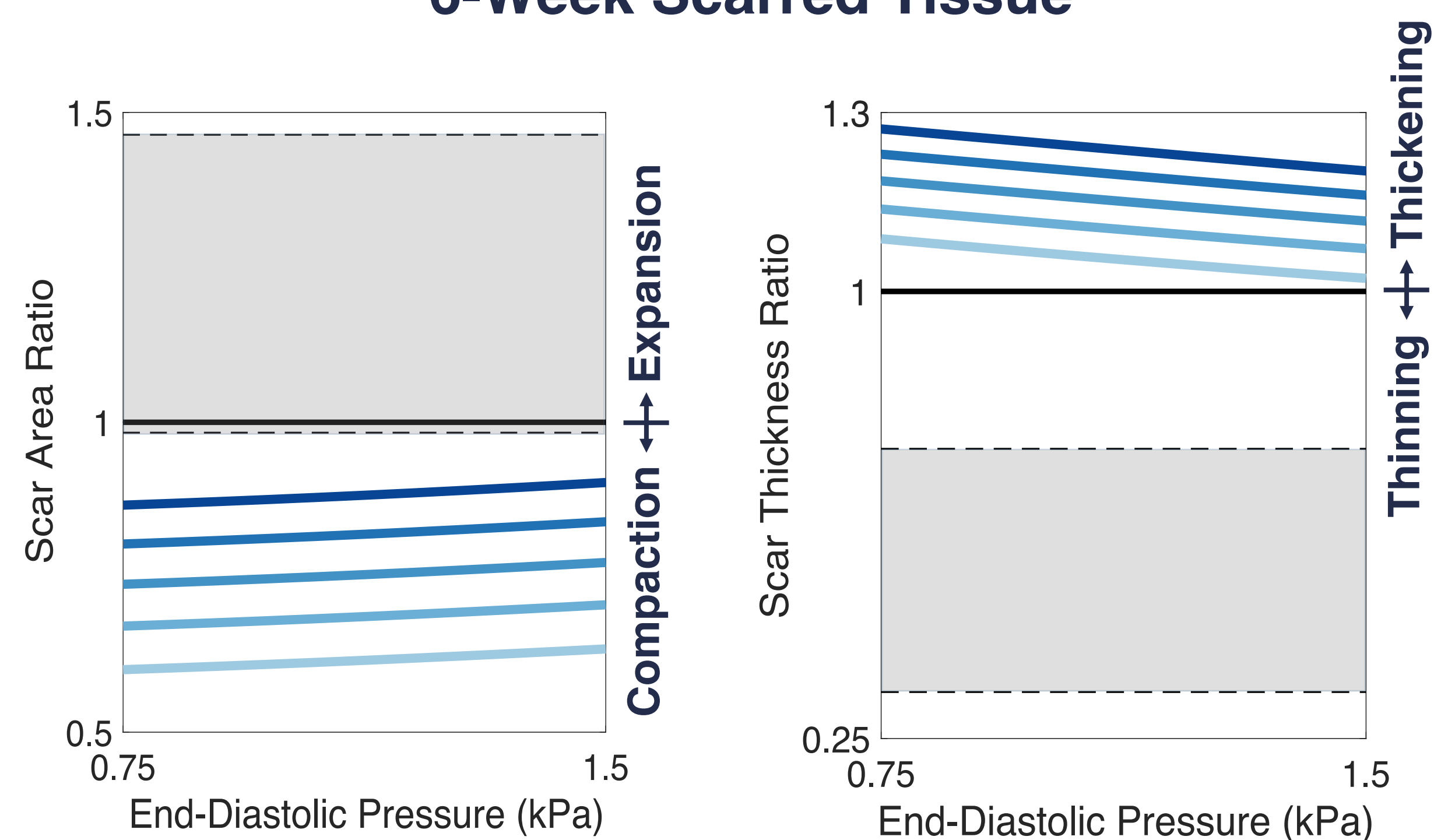
Results

Acute Ischemic Tissue

Observed *in vivo* Dimensions [4]

Scar Area Ratio vs End-Diastolic Pressure (kPa) — 0.75 to 1.5

Compaction ←→ Expansion

100% Volume
90% Volume
80% Volume
70% Volume
60% Volume

Scar Thickness Ratio vs End-Diastolic Pressure (kPa) — 0.75 to 1.5

Thinning ←→ Thickening

- Isotropic volume loss produced apparent scar compaction or expansion depending on simulated EDP and amount of remaining scar volume (Left)
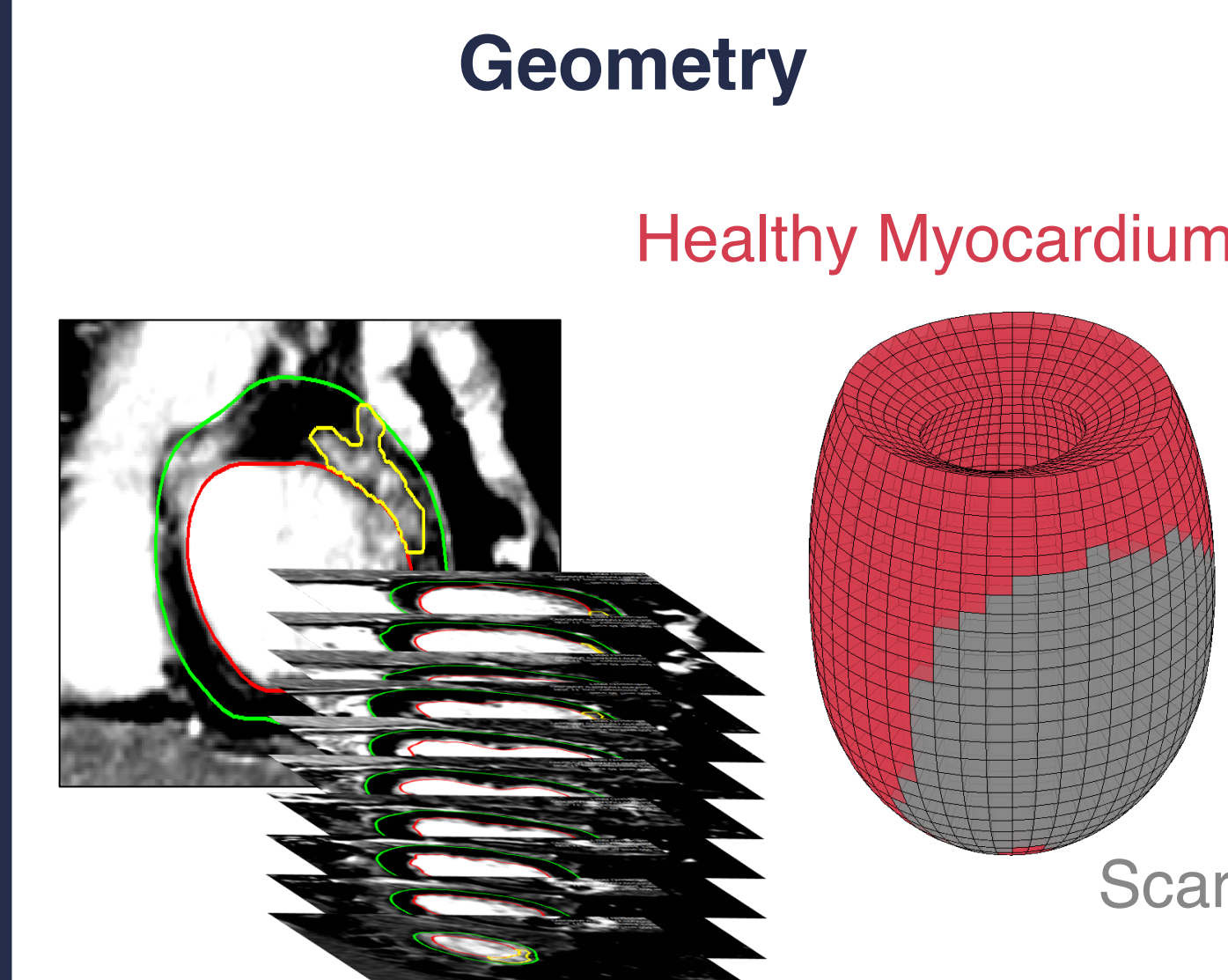- All cases predicted thinning of the scar (Right)

6-Week Scarred Tissue

Scar Area Ratio vs End-Diastolic Pressure (kPa) — 0.75 to 1.5

Compaction ←→ Expansion

Scar Thickness Ratio vs End-Diastolic Pressure (kPa) — 0.75 to 1.5

Thinning ←→ Thickening

- Simulations of isotropic volume loss predicted in-plane compaction at all diastolic pressures regardless of the extent of volume loss (Left)
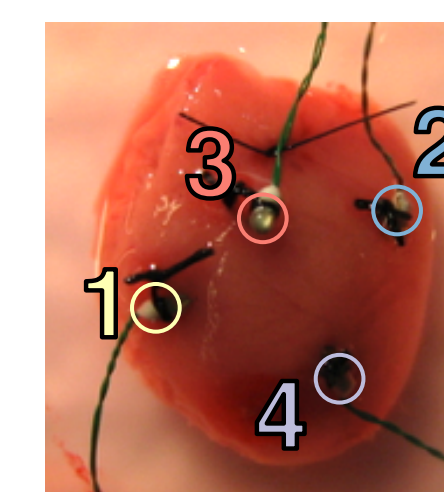- All cases predicted an increase in scar thickness at end-diastole (Right)

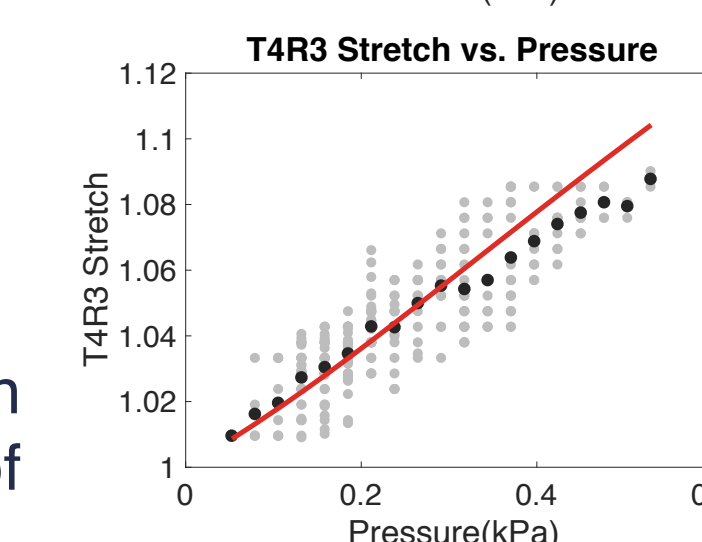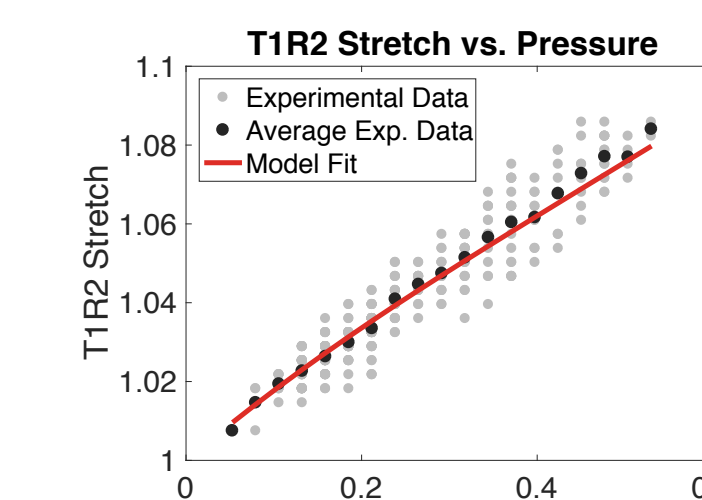## Methods

Finite Element Model Construction

Geometry

Healthy Myocardium

Scar

Material Behavior

Transversely Isotropic Mooney-Rivlin

T1R2 Stretch vs. Pressure
- Experimental Data
- Average Exp. Data
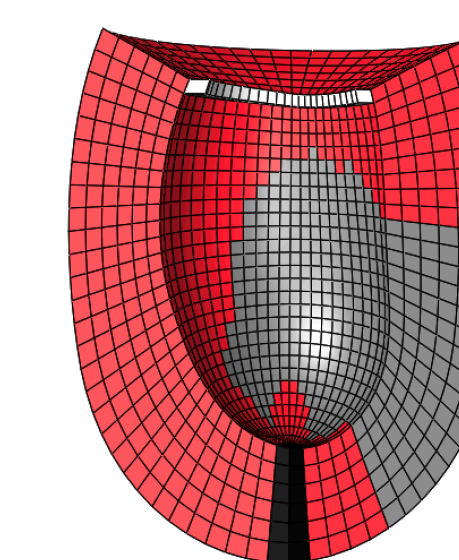- Model Fit

T4R3 Stretch vs. Pressure

The isotropic term of the material equation was increased to mimic the properties of rat infarct scar 6 weeks post-MI [2]
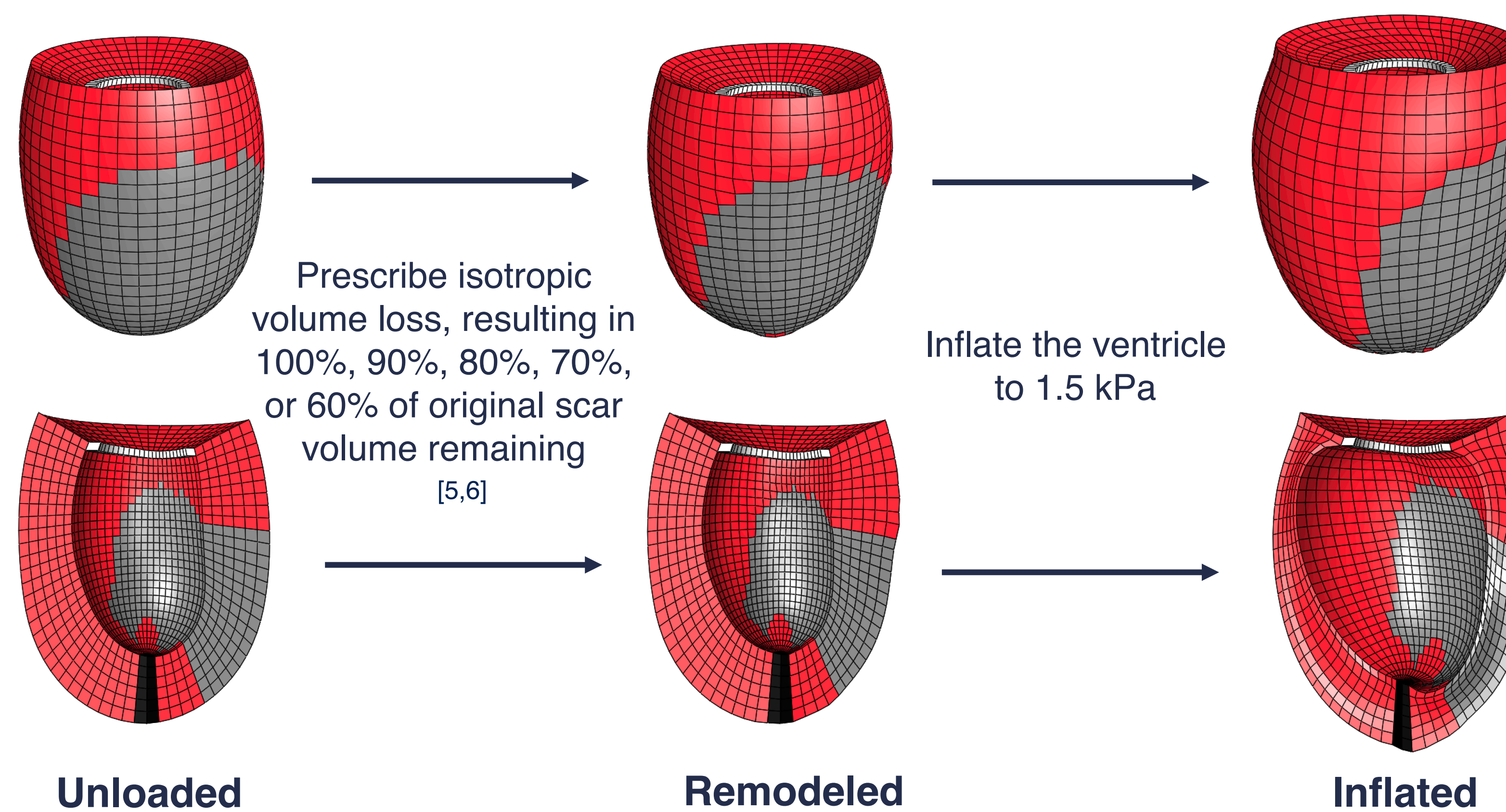
Boundary Conditions

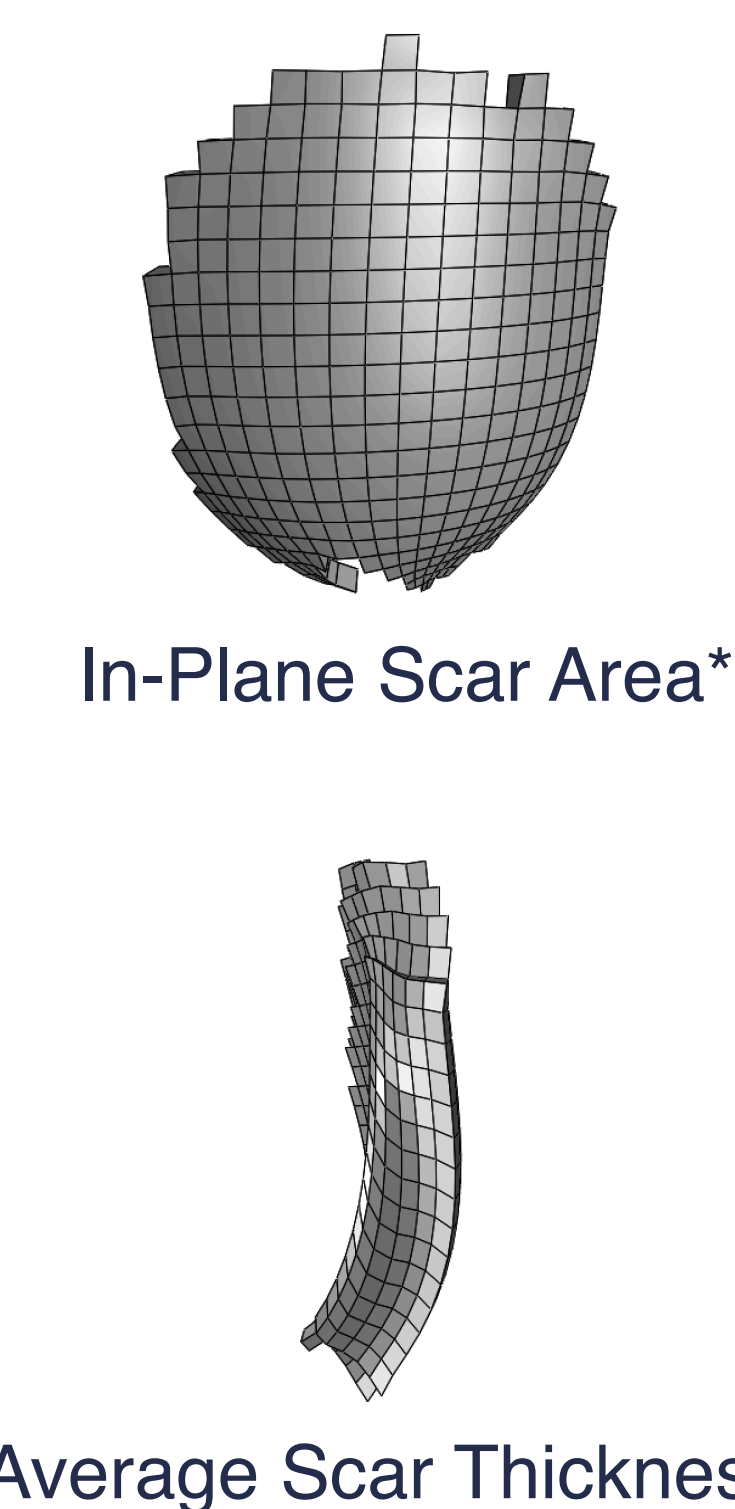The displacements of basal surface nodes were fixed longitudinally

The valve ring (white) and apex (black) were modeled as rigid bodies:
- The valve ring is fixed in all directions
- The apex allowed to displace only in the longitudinal direction and rotate

Scar Remodeling Simulations

Prescribe isotropic volume loss, resulting in 100%, 90%, 80%, 70%, or 60% of original scar volume remaining [5,6]

Inflate the ventricle to 1.5 kPa

Unloaded   **Remodeled**   **Inflated**

Metrics

In-Plane Scar Area*

Average Scar Thickness*

*Normalized to respective values in the non-remodeled scar at an EDP of 0.75 kPa

Discussion

- The simulations provide strong evidence that the assumption of isotropic volume loss is inconsistent with available data which raises interesting questions about how to model the replacement of muscle by scar in three dimensions.
- Modeling at the level of the individual proteins and components may be necessary to understand the packing of these elements in the tissue.
- These questions have potentially important **therapeutic implications**, since increasing wall thickness may be the primary mechanism by which biomaterial injections limit adverse remodeling of the LV following infarction [7].

Model Limitations

1. Increasing only the isotropic term within the scar material does not allow us to precisely match previously published biaxial testing data on infarct scar.
2. Only one representative infarct geometry was used in the simulations; infarcts of different size, location, and transmurality may exhibit different loaded dimension changes.
3. In-plane area ratio is calculated in this study but is compared to normalized in-plane dimension changes from studies that reported a variety of infarct measurements.

Acknowledgements

References

[1] Sharpe, N, *Am J Cardiol*, 70:20-6, 1992.
[2] Fomovsky, G and Holmes, J, *Am J Physiol-Heart C*, 298.1:H221-H228, 2009.
[3] Fishbein, M et al., *Am J Pathol*, 90:57-70, 1978.
[4] Richardson, W and Holmes, J, *J Cardiovasc Transl*, 8.7:421-430, 2015.
[5] Maas, S et al., *J Biomech Eng*, 134.1:011005, 2012.
[6] Rodriguez, E et al., *J Biomech*, 27.4:455-467, 1994.
[7] Kelley, S et al., *Circulation* 99.1:135-142, 1999.